Smart, Injury-Triggered Therapy for Ocular Trauma

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PUBLIC ABSTRACT

Traumatic eye injury is one of the leading causes of blindness in military personnel and young males worldwide. Frequently as a result of ocular injury, a complication develops known as proliferative vitreoretinopathy (PVR). This is a process that is very similar to wound healing and scar formation know as intraocular fibrosis, often a primary reason for the loss of vision after ocular trauma. PVR is a complex process initiated by harmful processes such as inflammation, loss of blood supply, and even bleeding within the eye cavity known as vitreous. The eye injury can initiate the proliferation and migration of inflammatory cells in the sensory part of the eye, the retina, and the support cells of the eye known as pigment epithelium (RPE) cells, which then contribute to the formation of membrane-like structures in the eye vitreous that contract and detach the retina from RPE that can cause significant loss of vision.

Our proposal will focus on special enzymes, called proteases, that digest proteins and change the cellular environment in the retina. Many pathological events in the eye can be traced to the local pro-inflammatory processes that trigger several downstream mechanisms including the activation of proteases, enzymes that cleave proteins in and around the cells of the retina. We propose a strategy to develop transmembrane proteins that can be delivered in the eye, specifically designed to release therapeutic proteins at the site of injury after being cleaved by proteases activated after traumatic eye injury. Our group has developed a way to change these proteases so that instead of harmful they can now release therapeutic proteins. Once inserted into the cell membrane of retinal cells, these sensors can be activated by the injury to release therapeutics in the eye and help to avoid loss of vision after injury.

Considering the significant personal, medical, and socioeconomic impact of blindness due to ocular trauma, there is a pressing need for novel treatments. Traumatic eye injuries require immediate surgical intervention to prevent vision loss, and our goal is to also improve the outcome of the surgery by developing a powerful, prophylactic, and locally acting treatment to enable retinal cells to release their own anti-inflammatory and antiproliferative proteins to prevent the formation of PVR and loss of vision. It is important that the therapeutic proteins are only released when and where they are needed so as to minimize any systemic and local side effects. We plan to develop ways to make these proteases release therapeutic "agents" only when and where a damaging inflammatory event occurs in the eye.

This strategy can be further applied as prophylactic treatment for patients with surgeries for retinal detachment frequently complicated with PVR. Since the release of protective proteins does not need any intervention once the agents are given in advance, this may also apply to soldiers scheduled for military combat and field operations with high risk for injury, when they are alone, unconscious, or far away from any medical institution and when help is not immediately available.